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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,356	09/02/1999	DARIO NERI	515-4132	3100

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/194,356	NERI ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-47,53-55 and 57-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-47,53-55 and 57-61* is/are rejected.

7)☒ Claim(s) *38-42 and 46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 07, 2006 has been entered.

2. Claims 30-47, 53-55 and 58-61 are pending.

Claims 30-47, 53-55 and 58-61 are examined on the merits.

Sequence Compliance

3. The disclosure is no longer objected to because of the specification does contain nucleic acid sequences with identifying SEQ. ID. Numbers, see page 24, lines 15-17, 22 and 23, see Remarks submitted December 28, 2000.

Maintained Rejections and New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The entire claim is vague and indefinite. It is not clear how an antibody can comprise another antibody such as CGS-1 or CGS-2. Applicants are requested to clarify.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The rejection of claims 30-37, 43, 55, 57, 59 and 60 under 35 U.S.C. 102(b) as being anticipated by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005 is maintained. Applicants have provided a 1.132 declaration submitted by March 7, 2006 by the main inventor, Dr. Sekiguchi asserting the Japanese patent in not enabling for production for an antibody binding to the ED-B domain of FN. Dr. Sekiguchi asserts the anticipatory antibody appeared to bind the ED-B domain, but further testing was shown that it did not bind. The declaration has been carefully reviewed and considered, as well as the arguments and assertions therein, but found to be unpersuasive.

JP(A) H2-76598 discloses a monoclonal antibody, which specifically recognizes the ED-B domain comprising 91 amino acids, see page 2, first and third paragraph.

These amino acids are the same as the ED-B domain of Applicants. The statements within the declaration, particularly those found on page 2, second full paragraph are speculative and unsupported. Applicants should provide objective scientific evidence along with the declaration to substantiate the statements of record, i.e. laboratory notes, scientific results. See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Moreover, the declaration states "...OAL-CF525 is not directed to the EDB domain per se, but rather recognizes an undefined epitope produced by the insertion of EDB between III-7 and III-8 domains", see Declaration, page 2, last sentence. When this statement is reviewed within the context of the entire paragraph it is not clear that the antibody did not bind directly to the ED-B oncofoetal domain of FN. Applicants are requested to clarify these alleged results. Applicants may want to submit a drawing, Western blot data or some scientific evidence aiding in the understanding of the statements of record. For the reasons of record and the analysis provided above the rejection is maintained.

8. The rejection of claims 30-37, 43, 47, 55, 57 and 59-61 under 35 U.S.C. 102(b) as being anticipated by JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005 is maintained. Applicants' arguments have been presented in the first cited 102(b) rejection. Applicants do note the OAL-pF115 antibody is not an antibody of the invention listed in the patent, but rather a control

antibody. This fact has been duly noted. These points of view and assertions have been carefully reviewed, but found unpersuasive.

The Examiner's position for this rejection is the same for the first cited 102(b) rejection and the rejection is maintained for the reasons of record.

9. Claims 30-32, 34-37, 43, 47, 53, 55 and 57-61 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent number 4,894,326 (issued January 16, 1990/ IDS reference 1, submitted August 15, 2005). U.S. Patent 4,894,326 discloses an IgG1 monoclonal antibody (FDC-6), which defines the oncofoetal structure within fibronectin, see column 2, lines 41-47 and 60-63; and column 3, lines 2-8. The patent discloses the FDC-6 and other immunological binding partners such as antigen-binding fragments and chimearas comprised in a suitable carrier and introduced into the body of a mammal, see bridging paragraph of columns 4 and 5. "The FDC-6 antibody, as well as other antibodies raised against the oncofoetal structure, can be packaged in kits useful for assaying the presence of oncofoetal fibronectin", see column 5, lines 39-44. Inherently, the disclosed antibody has all the properties as deemed by the antibody or antibody fragment which binds directly to an ED-B oncofoetal domain of fibronectin (FN).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The rejection of claims 30-37, 43-45, 55, 57-59 and 60 under 35 U.S.C. 103(a) as being unpatentable over JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988) is maintained for the reasons of record.

12. The rejection of claims 30-37, 43-45, 47, 55 and 57-61 under 35 U.S.C. 103(a) as being unpatentable over JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988) is maintained for the reasons of record.

13. The rejection of claims 30-37, 43, 47 and 53-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988), in view of Clackson et al. (Nature 352:624-628, August 15, 1991) is maintained for the reasons of record.

14. The rejection of claims 30-37, 43, 47, 54, 55, 57 and 59-61 under 35 U.S.C. 103(a) as being unpatentable over JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005, in view of Clackson et al. (Nature 352:624-628, August 15, 1991) is maintained for the reasons of record.

15. The rejection of claims 30-37, 43, 53, 55, 57, 59 and 60 under 35 U.S.C. 103(a) as being unpatentable by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005 is maintained for the reasons of record.

16. The rejection of claims 30-37, 43, 53, 55, 57, 59 and 60 under 35 U.S.C. 103(a) as being unpatentable by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005 is maintained for the reasons of record.

17. Claims 30-32, 34-37, 43-45, 47, 53, 55 and 57-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 4,894,326 (issued January 16, 1990/ IDS reference 1, submitted August 15, 2005), and further in view of in view of Bird et al. (Science 242:423-242, 1988) and Clackson et al. (Nature 352:624-628, August 15, 1991). The teachings of the patent have been discussed in the 102(e) rejection above. The aforementioned reference does not teach that the antibody is single-chain Fv molecule (scFv) or a dimeric scFv.

However, Bird teaches the production of single-chain fragments, dimeric scFV and the efficacy of single-chain antibodies. And Clackson teaches the production of single-chain fragments utilizing a random combinatorial library. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to produce single-chain antibodies and by-pass hybridoma technology and animal immunization to implement phage display to produce single-chain antibodies, which are high-affinity antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all references that single-

chain antibodies are advantageous because of their small size, lower background in imaging applications, less immunogenic and ability to penetrate the microcirculation surrounding solid tumors better.

Allowable Subject Matter

18. Claims 38-42 and 46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

19. Claims 38-42 and 46 are free of the art.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
20 March 2006